REMARKS

Reconsideration of the present application is respectfully requested in view of the above amendments and the following remarks. These amendments and remarks are being filed with a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114.

Claims 1-14 are pending; claims 1-7 and 13-14 are currently under examination, and claims 8-12 are withdrawn for being directed to non-elected subject matter. Without acquiescence or prejudice, claim 1 is amended to particularly point out and distinctly claim certain embodiments of Applicants' invention, claim 14 is canceled, and new claim 15 is added. No new matter has been added by the amendments. Support for the amendments can be found in the specification as filed, for example, at page 33, lines 6-14.

REJECTIONS UNDER 35 U.S.C. § 102

Claims 1, 2, 7, and 13 stand rejected under 35 U.S.C. § 102(b) for alleged lack of novelty over Maddon *et al.* (U.S. Patent No. 6,034,223). The Examiner asserts that Maddon *et al.* disclose a human Fc region chemically linked to a non-peptide toxin via site specific linkage through the N-linked sugar residues present on the Fc region. The Examiner then alleges that the structural features of the instant claims read on the molecule of Maddon *et al.*

Applicants traverse this rejection and submit that the instant claims satisfy the requirements of novelty over Maddon *et al.* Embodiments of the instant claims relate, in pertinent part, to an IgG Fc fragment as a drug carrier, or a combination thereof or a hybrid thereof, wherein the Fc fragment is covalently linked to a drug through a non-peptide linker, wherein the non-peptide linker comprises polyethylene glycol, polypropylene glycol, copolymers of ethylene glycol and propylene glycol, polyoxyethylated polyols, polyvinyl alcohol, dextran, polyvinyl ether, polylactic acid (PLA), polylactic-glycolic acid (PLGA), a lipid polymer, a chitin, hyaluronic acid, or a combination thereof.

Maddon *et al.* fail to disclose each feature of the instant claims. For instance, Maddon *et al.* fail to disclose an Fc-based drug carrier that is linked to a drug via a ***non-peptide linker***, as specified in the instant claims. Indeed, nowhere does this reference disclose an Fc fragment that is covalently linked to a drug through polyethylene glycol, polypropylene glycol,

copolymers of ethylene glycol and propylene glycol, polyoxyethylated polyols, polyvinyl alcohol, dextran, polyvinyl ether, polylactic acid (PLA), polylactic-glycolic acid (PLGA), a lipid polymer, a chitin, hyaluronic acid, or a combination thereof. In this manner, Maddon *et al.* fail to anticipate the instant claims.

Given the deficiencies in Maddon *et al.*, Applicants submit that the instant claims satisfy the requirements of novelty over this reference, and respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 102(b).

REJECTIONS UNDER 35 U.S.C. § 103

Claims 1-7 and 13 stand rejected under 35 U.S.C. § 103(a) for alleged obviousness over Maddon *et al.* in view of Presta (U.S. Patent No. 6,737,056). The Examiner essentially relies on Maddon *et al.* as noted above, but agrees that this reference does not teach aglycosylated IgG4 Fc fragments. However, the Examiner asserts that Presta teaches a human IgG4 region with reduced effector function that can be produced in *E. coli*, and which allegedly has the same sequence as SEQ ID NO:8. The Examiner also asserts that the *E. coli* produced IgG4 would be aglycosylated, because it is known that *E. coli* lacks glycosylation enzymes. The Examiner then asserts that it would have been obvious to substitute the IgG2 Fc region of Maddon *et al.* with the human IgG4 region of Presta.

Applicants traverse this rejection and submit that the instant claims satisfy the requirements of non-obviousness. In particular, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness. *See In re Mayne*, 104 F.3d 1339 (Fed. Cir. 1997) (The USPTO has the burden of showing a *prima facie* case of obviousness).

At a minimum, it must be demonstrated that the combined references teach or suggest all the claim features, and even assuming, *arguendo,* that the combination of references teaches each claim feature, the Examiner must provide an explicit, apparent reason to combine these features in the fashion claimed by the Applicant with a reasonable expectation of success. *See KSR v. Teleflex, Inc.,* No. 04-1350 at 4, 14 (U.S. Apr. 30, 2007) ("A patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art").

The cited references ***in combination*** fail to teach or suggest each feature of the instant claims. As discussed in the section 102(b) rejection above, Maddon *et al.* fail to teach or suggest an Fc-based drug carrier that is linked to a drug via a ***non-peptide linker***, as specified in the instant claims. Specifically, nowhere does this reference even remotely suggest an Fc fragment that is covalently linked to a drug through polyethylene glycol, polypropylene glycol, copolymers of ethylene glycol and propylene glycol, polyoxyethylated polyols, polyvinyl alcohol, dextran, polyvinyl ether, polylactic acid (PLA), polylactic-glycolic acid (PLGA), a lipid polymer, a chitin, hyaluronic acid, or a combination thereof. Presta does not remedy the deficiencies in Maddon *et al.*, because this reference is entirely silent as to an Fc fragment covalently linked to a drug through a ***non-peptide linker***, as specified above and in the instant claims. In failing to teach or suggest each feature of the instant claims, the cited references, alone or ***in combination***, fail to establish the minimal elements of a *prima facie* case of obviousness.

These references also fail to provide any apparent reason to practice the presently claimed subject matter with a reasonable expectation of success. Rather, since the cited references do not teach or suggest an Fc fragment covalently linked to a drug through a non-peptide linker, as specified in the instant claims, persons of ordinary skill in the art at the time of invention would have had no reason whatsoever to practice the instant molecules. Given the deficiencies in the cited references, such persons would have had to embark on a whole new line of experimentation to arrive at the presently claimed subject matter, such as by attaching a non-fusion Fc fragment to a drug via a ***non-peptide linkage*** (*e.g.,* polyethylene glycol, polypropylene glycol, copolymers of ethylene glycol and propylene glycol), as recited in the instant claims. This new line of experimentation cannot be found in either Maddon *et al.* or Presta, nor can any expectation or prediction of its success, as empirically demonstrated by Applicants. Accordingly, the cited references not only fail to provide any apparent reason to practice the presently claimed Fc-based drug molecules, but fail as well to provide the requisite reasonable expectation of success. Applicants, therefore, submit that the cited references do not establish a *prima facie* case of obviousness over the instant claims.

Given the fact that the cited references in combination fail to establish the minimum elements of a *prima facie* case of obviousness, Applicants submit that the instant claims satisfy the requirements of nonobviousness over these references, and respectfully request withdrawal of this rejection under 35 U.S.C. § 103(a).

OBVIOUSNESS TYPE DOUBLE PATENTING

The Examiner ***provisionally*** rejected claims 1-7 and 13 for alleged obviousness-type double patenting over claims 1-13 of co-pending U.S. Application No. 10/535,231. The Examiner also ***provisionally*** rejected claims 1-7 and 13 for alleged obviousness-type double patenting over claims 1-19 and 27-44 of co-pending U.S. Application No. 10/535,232.

Applicants traverse these rejections. Nonetheless, since these rejections are ***provisional***, Applicants will address the rejections upon allowance of a claim set in either this application, or the above-noted co-pending applications.

Applicants believe that all of the claims in the application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

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